Exhibit A

Graft-versus-host disease

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Graft-versus-host disease (GVHD) is a complication that can occur after a bone marrow transplant in which the newly transplanted material attacks the transplant recipient's body.

See also: Transplant rejection

Causes

GVHD occurs in a bone marrow transplant involving a donor and a recipient. The bone marrow is the soft tissue inside bones that helps form blood cells, including white cells that are responsible for the immune response. Since only identical twins have identical tissue types, a donor's bone marrow is normally a close, but not perfect, match to the recipient's tissues. See: Histocompatibility antigen test

The differences between the donor's marrow and recipient's tissues often cause T cells (a type of white blood cells) from the donor's marrow to recognize the recipient's body tissues as foreign. When this happens, the newly transplanted bone marrow attacks the transplant recipient's body.

Acute GVHD starts within the first 3 months after transplant. Chronic GVHD starts more than 3 months after transplant, and can last for 3 years or longer.

Rates of GVHD vary from between 30-40% among related donors and recipients to 60-80% between unrelated donors and recipients. The greater the mismatch between donor and recipient, the greater the risk of GVHD. After a bone marrow transplant, the recipient usually takes drugs that suppress the immune system, which helps reduce the chances (or severity) of GVHD.

Symptoms

Symptoms in both acute and chronic GVHD range from mild to severe.

Common acute symptoms include:

- Abdominal pain or cramps
- Diarrhea
- Fever
- Jaundice
- Skin rash
- Vomiting
- Weight loss

Chronic symptoms may include:

- Dry eyes and dry mouth
- Hair loss
- Hepatitis
- Lung and digestive tract disorders
- Skin rash

In both acute and chronic GVHD, the patient is very vulnerable to infections.

Exams and Tests

The tests done usually depend on the symptoms, but may include:

- Gastrointestinal endoscopy, with or without a biopsy
- Liver function tests (AST, ALP, and bilirubin levels will be increased)
- Liver biopsy (if the patient only has liver symptoms)
- Lung x-rays
- Skin biopsy

Treatment

The goal of treatment is to suppress the immune response without damaging the new marrow. Medicines commonly used include methotrexate and cyclosporine, either alone or in combination.

High-dose corticosteroids are the most effective treatment for acute GVHD. Antibodies to T cells are given to patients who do not respond to steroids.

Treatment of chronic GVHD includes prednisone (a steroid) with or without cyclosporine. Other treatments include mycophenolate mofetil (CellCept) and tacrolimus (Prograf).

Outlook (Prognosis)

How well a person does depends on the severity of the condition. Some cases of GVHD can lead to death.

Many cases, whether acute or chronic, can be treated successfully. Sometimes treatment of the condition can lead to severe complications.

Successful treatment of GVHD does not guarantee that the bone marrow transplant itself will succeed in treating the original disease.

Possible Complications

- Cholestasis
- Moderate-to-severe damage to the liver, lung, or digestive tract
- Severe infection
- Severe lung disease

When to Contact a Medical Professional

If you have had a bone marrow transplant and are no longer in the transplant center, call your health care provider immediately if any unusual symptoms appear, including:

- Diarrhea
- Difficulty breathing
- Skin rash
- Stomach cramps
- Yellowing of the skin or eyes (jaundice)

Prevention

Before a transplant, your blood type and tissue type will be carefully matched with eligible donors. This matching will reduce the risk of GVHD. Whenever possible, donations from closely matched family members can further decrease the risk of this problem. Absolute prevention of GVHD is not possible - it is a risk with any bone marrow transplant.

Alternative Names

GVHD

References

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